3.4 Paper IV: Preventive Intervention for Trauma Reactions in Young Injured Children: Results of a Multi-Site Randomised Controlled Trail

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Summary

Background Young children are at particular risk for injury. 10 – 25% develop post-traumatic stress disorder (PTSD). However, no empirically supported preventive interventions exist. Therefore, this study evaluated the efficacy of a standardized targeted preventive intervention for PTSD in young injured children.

Methods Injured children (1 – 6 years) were enrolled in a parallel-group superiority prospective randomised controlled trial (RCT) in Australia and Switzerland. Screening for PTSD-risk occurred 6 – 8 days post-accident. Children were randomised to a 2-session CBT-based intervention or treatment as usual (TAU). Primary outcome was change in PTSD symptom (PTSS) severity from 2-weeks, to 3- and 6-months using blinded assessments. Secondary outcomes were change in PTSD diagnosis, functional impairment, and behavioural difficulties. Trials were registered with the Australian New Zealand Clinical Trials Registry (ACTRN12614000325606) and ClinicalTrials.gov (NCT02088814). Trial status is complete.

Findings During June 2014 – July 2016 (Australia) and April 2014 – May 2017 (Switzerland), 133 children screened 'high-risk' and were assigned to intervention (n = 62) or TAU (n = 71). Multilevel intention-to-treat analyses revealed a significant intervention effect on PTSS severity over time (t = 3.08, p = .003). At 3-months, intervention children showed significantly less PTSS severity than control children, indicating a medium effect (p = .009; Cohen's d = 0.51). This was not the case at 6-months (p = .335). Mean differences between groups were -6.28 (-10.99 to -1.57; p=.009) at 3-months and -2.07 (-6.30 to 2.16; p=.335) at 6-months. On secondary outcomes, multilevel analyses revealed significant treatment effects over time regarding PTSD diagnosis (z = -11.08, p < .001), functional impairment (z = -2.50, p = .012), and behavioural difficulties (t = 3.09, p = .003).

Interpretation This multi-site RCT provides worldwide first evidence for the efficacy of a targeted preventive intervention for PTSD in children ≤6 years leading to a quicker relief from trauma reactions. This has important implications for young children's acute clinical treatment and fast recovery after single-event trauma.

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Introduction

Injury is a particularly common potentially traumatic event experienced by young children (<6 years; WHO, 2008). The majority of young children are resilient and only experience transient acute distress, however, 10–25% develop posttraumatic stress disorder (PTSD), anxiety, and/or behavioural disorders within 1–6 months post-injury. For 2.4 – 13% of children, untreated traumatic stress reactions follow a chronic course for up to 3-years (De Young et al., 2011a; Meiser-Stedman, Smith, Yule, et al., 2017). Early childhood represents one of the most vulnerable periods for physical, cognitive, social, and psychological development across the lifespan. Therefore, a trauma during this time can have far-reaching negative effects on children, families, and health and education systems (Haag et al., *in press*).

Pediatric medical trauma can also be very distressing for parents, with 25 – 45% experiencing elevated levels of guilt, acute stress, PTSD, depression, and anxiety over the first 6-months after a child's injury (Bakker, Maertens, et al., 2013; De Young et al., 2014). Parental distress and parenting behaviors (e.g. overprotectiveness, avoidance) can contribute the development and maintenance of child trauma symptoms (De Young et al., 2014; Williamson et al., 2017).

Despite this, the mental health needs of young traumatised children and their parents are still substantially underrecognized and underserviced (Segal et al., 2018). There is a need for targeted preventive interventions for young children at PTSD-risk following trauma. However, only one previous study has examined the efficacy of an early intervention at preventing PTSD and behavioural difficulties in young injured children (2 – 6 years), but failed to find significant differences between intervention and control (Kramer & Landolt, 2014). Therefore, prior to this study, there was no empirical evidence on early preventive interventions for PTSD in young children.

An international collaboration (Australia and Switzerland) was formed to develop a new targeted preventive intervention: Coping with Accident Reactions (CARE; De Young et al., 2016). The objective of this study was to investigate the efficacy of the CARE-intervention via two aligned randomised control trials (RCTs). It was hypothesised that children receiving the CARE-intervention would experience a significantly greater reduction in PTSD symptom (PTSS) severity (primary outcome), rates of PTSD diagnosis and

functional impairment, and behaviour difficulties (secondary outcomes) at 3- and 6-months post-injury compared to children who received treatment as usual (TAU).

Panel: Research in Context

Evidence before the study

Results from a 2011 meta-analysis of early interventions in children and adolescents exposed to single-event trauma were reviewed before study commencement. PubMed was searched for publications from 1 Jul 2011 – 1 Feb 2014 using the terms "(child OR children OR childhood) AND (early OR short OR brief) AND (intervention OR prevention OR treatment OR therapy) AND (posttraumatic OR PTSD OR stress OR distress) AND (trauma OR accident OR injury)", identifying four more recent RCTs. Existing literature provides limited and mixed evidence that early intervention can reduce PTSS in older children (7–16 years) after accidental trauma. However, the only study that evaluated an early intervention for young injured children (2 – 6 years) did not find significant effects.

Added value of this study

The CARE-intervention resulted from an international collaboration that considered current conceptual approaches, best available empirical evidence and consultation with leading experts in the field. CARE differs from previous unsuccessful interventions by having a parent focus and utilising developmentally appropriate therapeutic resources. This is the first study to demonstrate that it is possible to reduce and prevent persistent PTSS, PTSD, functional impairment, and behavioural difficulties in young children injured from various accidents and across two international sites in different languages (English and German). This study also obtained a good sample size with appropriate statistical power and had pre-specified standard methods for randomisation and analysis. The targeted preventive intervention has the potential to be widely applicable to different single-event traumas.

Implications of all the available evidence

The evidence base for early interventions for PTSD in children of all ages is scant and inconclusive. This study has important clinical and research implications as the results provide good evidence in support of providing a Cognitive-Behavioural-Therapy (CBT)-based preventive intervention to parents of children screening at 'high-risk' of developing PTSD within the first 2-weeks of a potentially traumatic accident. Future research needs to replicate these findings in other acute trauma settings and examine effectiveness and cost-effectiveness of the CARE-intervention when implemented into routine clinical practice.

Methods

Study design

The study design was a two-arm, parallel-group superiority prospective RCT comparing the CARE-intervention with TAU. The Consolidated Standards of Reporting Trials (CONSORT) guidelines for RCTs were followed. One RCT was conducted at the Lady Cilento Children's Hospital, Brisbane, Australia, and the other at the University Children's Hospital, Zurich, Switzerland. The Australian study obtained ethics approval from the University of Queensland Human Research Ethics Committee, and the Children's Health Queensland Human Research Ethics Committee. It was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12614000325606) on 26 March 2014. The Swiss study was approved by the Kantonale Ethikkommission Zürich and registered at ClinicalTrials.gov (NCT02088814) on 12 March 2014. The study protocol was published.[10]

Participants

Participants were eligible in Australia if the child (1) required inpatient or outpatient treatment for an unintentional burn injury or was admitted for ≥6 hrs following an unintentional injury (e.g., dog bite, road traffic accidents) and (2) was aged 1–6 years. Participants met eligibility criteria in Switzerland if the child (1) required inpatient or outpatient treatment for an unintentional burn and (2) was aged 1–4 years. Exclusion criteria were: (1) Parents' language ability was insufficient (English in Australia, German in Switzerland), (2) initial Glasgow Coma Scale score <12, (3) injury resulted from suspected abuse, (4) child under the care of child safety, (5) child had a pervasive developmental disorder, or (6) child expected to stay in the intensive care unit >1 week.

Randomisation and masking

A computerised random number generator was used by a researcher not involved in the study to create a randomisation list using blocks of four participants (Sealed Envelope Ltd., 2017). Concealment of group allocation was ensured by using a numbered series of opaque and sealed envelopes. Following baseline assessment, the interviewer opened the envelope to reveal assignment to treatment condition. The 3- and 6-months follow-up assessments were completed by different graduate psychologists who were blind to treatment condition.

Procedures

The study was embedded in a stepped-care procedure. The research team identified eligible families via hospital records and contacted them (in person or over the phone) within

one week of the child's accident. Written informed consent was obtained from all interested parents. Participating parents completed the PTSD-risk screen, either written or verbally, approximately 6–8 days post-accident (M = 7.44, SD = 2.11). Primary and secondary outcomes were assessed using standardised diagnostic interviews and questionnaires. On average, baseline interviews were conducted 12.66 (SD = 4.13) days after the accident. Immediately following baseline assessment, families were randomly assigned to either the intervention or control group. Session 1 of the intervention commenced immediately after randomisation. Session 2 took place one week after session 1. The control group received TAU. At both hospitals, TAU consisted of standard medical and psychosocial care. Follow-up interviews were conducted at 3-months (range 78 – 124 days) and 6-months (range 163 – 209 days) post-injury.

CARE intervention

The Coping with Accident Reactions (CARE) intervention was developed by researchers and clinical psychologists from Australia and Switzerland (De Young et al., 2016). CARE is an early targeted preventive intervention (i.e. provided within the first 2-weeks to children screened as 'high-risk' for developing PTSD; Kazak, 2006). It is a manualised two-session (45 – 60 min each), CBT-based intervention designed to be delivered by psychologists. CARE includes components of the early intervention by Kramer & Landolt (2014), as well as key elements hypothesised to be important for young children's psychological recovery. The sessions consist of (1) a trauma narrative, (2) psychoeducation on trauma reactions in young children and parents, (3) general coping strategies to manage acute distress, (4) provision of developmentally appropriate resources (i.e. owl toy and storybook), (5) monitoring of child and parent distress, (6) specific coping strategies for child's presenting problems, and (7) education about trauma-related parenting behaviours and identification of goals for change. CARE includes the option of completing two additional brief follow-up contacts (5 – 15 minutes) conducted either in person or via phone approximately 3-days after session 1 and 6-weeks post-accident. Refer to the study protocol for further information.[10] Treatment fidelity was ensured by having adequate training and regular supervision of therapists by the intervention developers, regular discussion amongst the two international teams and the use of checklists to ensure adherence to intervention protocol.

Outcome measures

To determine if children were at 'high-risk' of developing PTSD, the Pediatric Emotional Distress Scale-Early Screener (PEDS-ES) was used. The PEDS-ES is a 21-item

caregiver-report questionnaire designed to screen for elevated trauma-related behaviour in children aged 2 – 10 years. The PEDS-ES has demonstrated validity for predicting PTSD-risk in young children (2 – 6 years) following injury (Kramer, Hertli, & Landolt, 2013). A score ≥8 indicates 'high-risk' for developing PTSD. In this study, internal consistency of the PEDS-ES was acceptable (α = .73).

The primary outcome, PTSS severity, was assessed using the PTSD-module from the Diagnostic Infant and Preschool Assessment (DIPA). This is based on the 'PTSD for children 6 years and younger' diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5; APA 2013). The DIPA is a semi-structured diagnostic interview conducted with the primary caregiver of children aged 1–6 years and has demonstrated acceptable test-retest reliability (Scheeringa & Haslett, 2010). Prior to study commencement, the original author of the DIPA revised the question response format so that symptom severity ratings could be obtained (i.e. sum of symptom frequency and intensity ratings on a 5-point Likert scale [0 – 4]). Internal consistency was good in the present study (α = .87).

Secondary outcomes for the study were PTSD diagnosis rates, functional impairment and behavioural difficulties. The DIPA was also used to diagnose PTSD and functional impairment (APA, 2013). A PTSD symptom was endorsed if its frequency was rated ≥1 and its intensity ≥2. Functional impairment was met if the child showed impairment in at least one of the five following domains: relationships with parents, siblings, peers, daycare providers, ability to act appropriately outside home, and child distress. The Child Behavior Checklist for ages 1.5–5 years (CBCL/1.5-5) is a 100-item parent-report checklist and was used to provide a measure for total internalising and externalising behaviour difficulties. The CBCL/1.5-5 has been widely used and demonstrated good psychometric properties (Achenbach & Rescorla, 2000). Internal consistency was excellent in the current study (α = .95). Demographic information was obtained from questionnaires completed at baseline. Medical data was collected from patient medical records. Injury Severity Scores (ISS) were calculated based on the Abbreviated Injury Scale, a widely used tool for rating injury severity in patients with scores ranging from 1 – 75 (Gennarelli & Wodzin, 2008).

Statistical analysis

Based on previous research on early interventions in injured children (Kramer & Landolt, 2014; Zehnder et al., 2010), medium effect sizes were estimated with regard to PTSS and behaviour difficulties. A power analysis (α = .05, Power = .80, Cohen's $d = 0.5$) using the G*Power software indicated a required sample size of n=51 for each of the two

groups to detect significant group differences in continuous variables (Faul, Erdfelder, Lang, & Buchner, 2007). With regard to group differences in dichotomous variables, the corresponding required sample size was $n = 44$ per group. The intent-to-treat sample was used for all analyses. Data were analysed using SPSS version 22 and R version 3.5.1 with the *lme4* (1.1-17) package (Bates, Mächler, Bolker, & Walker, 2015; IBM Corp., 2013; R Core Team, 2014). Comparisons between the two study sites and groups were performed with Student's t-tests for continuous data and Pearson χ^2 analysis for categorical variables. All tests were two-tailed. Mean differences, Odds ratios and effect sizes (Cohen's *d*) were computed regarding group differences in primary and secondary outcomes.

Multilevel modelling was used to investigate group differences in PTSS severity and behavioural difficulties over time due to nesting of repeated observations (level 1) within participants (level 2). For each model, treatment group, time (linear and/or quadratic) and the group x time interaction were included as fixed effects predictors. In order to control for site differences between Australia (AUS) and Switzerland (CH; **Table 13**), the variable site (AUS or CH) was also included as a fixed effect. Considering current methodological discussion (Feaster, Mikulich-Gilbertson, & Brincks, 2011) and to test if treatment outcomes differed between the two sites, we also ran the models including the site x group interaction. For both PTSS severity and behavioural difficulties, the site x group interaction did not have a significant effect ($p = .876$ and $p = .735$) nor change the models significantly ($\chi^2 = 0.03$, $p = .876$ and $\chi^2 = 0.11$, $p = .735$). Therefore, it was decided to not include the site x group interaction. A random intercept was included to allow individuals to vary in their mean outcome value. A random slope for time was included if it improved the model significantly. In order to test the effect of the intervention on categorical outcome variables (PTSD diagnosis, functional impairment), binary logistic multilevel regression analyses were computed. Multilevel modelling is robust to missing data due to dropout and does not exclude participants with missing data at some measurement time points. Therefore, no replacement or imputation of missing data was conducted.

Role of the funding source

The funders of this research had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The authors had full access to all the data in the study and the corresponding author had final responsibility for the decision to submit for publication.

Results

Between 3 June 2014 – 31 July 2016, 726 eligible patients were identified and invited to participate in the Australian study. During the recruitment of the Swiss trial, 332 eligible patients were identified and approached between 1 April 2014 – 31 May 2017. Participant flow is illustrated in *Figure 7*. For both sites combined, 588 parents (56%) completed the screen within the required time-frame, of which 160 children (27%) screened 'high-risk', therefore qualifying for baseline assessment and randomisation to treatment condition. The final combined study sample consisted of 133 families of which 62 children were assigned to the intervention group and 71 to the control group (*Figure 7*). 57 (91.9%) of the families completed both treatment sessions. Reasons for non-completion of the second session included four parents reporting it was not needed as their child was coping fine and one family was unable to be contacted. The intervention was mostly completed by mothers (n = 48, 77.4%), followed by both parents (n = 5, 8.1%). 21 (58%) of the sessions were completed via phone (vs face-to-face) in Australia due to many families living a large distance (>1hour) from the hospital. Of the 133 children randomised, 28 (21.1%) did not complete the follow-up interviews: 12 (19.4%) from the intervention and 16 (22.5%) from the control condition. Assessment non-completion at 3- and 6-month follow-up was mainly due to families not being able to be reached after three attempts (*Figure 7*).

Participant's baseline demographic and medical characteristics for both treatment groups and both study sites are presented in **Table 13**. In the combined sample, 82.0% of children were ≤4 years with a mean age of 2.78 years (SD = 1.50, range 1.00 – 6.70). The majority of injuries were burns (n = 90, 67.7%). The Australian sample had a variety of injuries (e.g. laceration, crushing, drowning, dog bites, head or internal organ injury) with burns (n = 33, 43.3%) and fractures (n = 24, 31.6%) being most prevalent. Significant differences between Australia and Switzerland were found regarding child, mother and father age, child ethnic groups, maternal education, in- or outpatient treatment, and injury severity (see **Table 13**). Baseline outcome variables (PTSS severity, PTSD diagnosis, functional impairment, total behaviour difficulties) were also compared in both sites. A significant difference for total PTSS severity was found, with the Swiss sample reporting higher scores (AUS M = 20.41, SD = 12.88 and CH M = 30.44, SD = 16.31; t = -3.87, p = .000).

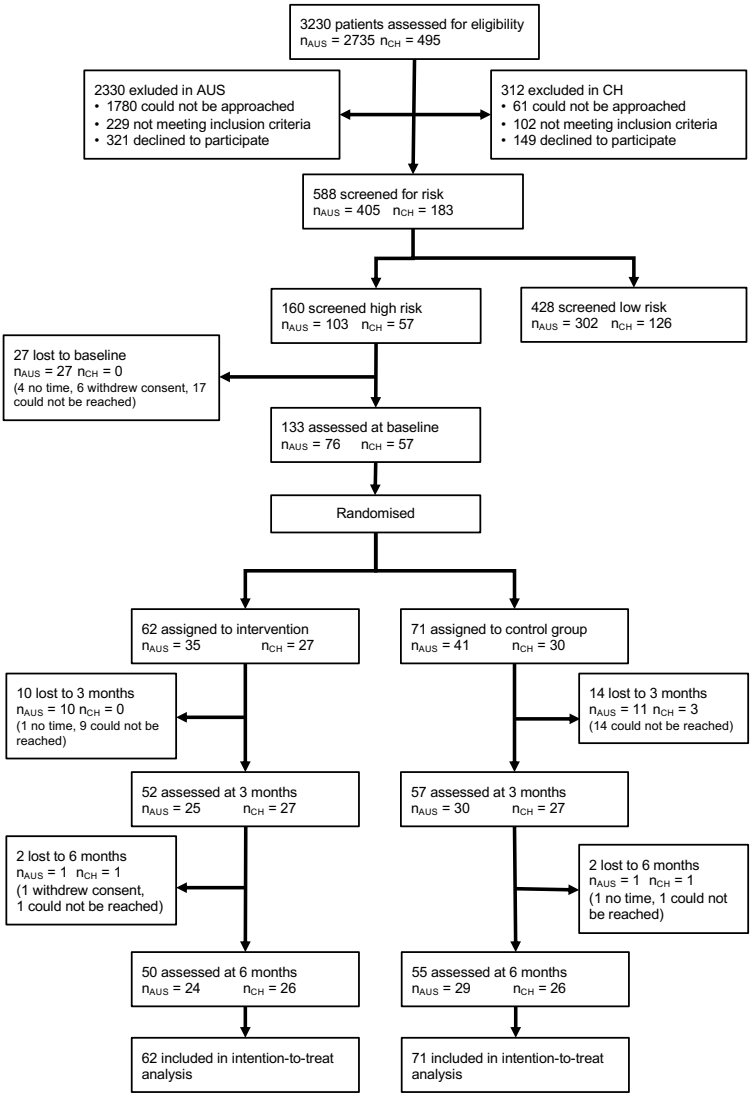

Figure 7. Participant flow.

Table 13

Comparison of demographic and medical characteristics: Australia versus Switzerland and intervention versus control group

Characteristics	Australia (n = 76)		Switzerland (n = 57)		t or χ^2	p	Intervention (n = 62)		Control (n = 71)		Combined sample (N = 133)	
	M (SD) or N (%)		M (SD) or N (%)				M (SD) or N (%)		M (SD) or N (%)		M (SD) or N (%)	
Child Age (years)	3.20	(1.75)	2.22	(.78)	4.32	.000	2.82	(1.48)	2.75	(1.52)	2.78	(1.50)
Range		1.10-6.70		1.00 – 4.25				1.08 – 6.70		1.00 – 6.70		1.00 – 6.70
Child Female Sex	40	(52.6)	26	(45.6)	.64	.423	30	(48.4)	36	(50.7)	66	(49.6)
Mother Age (years)	33.34	(6.54)	37.43	(5.07)	-3.89	.000	34.55	(6.06)	35.53	(6.51)	35.05	(6.26)
Father Age (years)	35.55	(6.24)	41.02	(5.86)	-4.71	.000	38.05	(6.20)	37.88	(7.10)	37.96	(6.64)
Child ethnic group					13.50	<.001						
Anglo/European	54	(71.1)	55	(96.5)			51	(82.3)	58	(81.7)	109	(82.0)
Non-Anglo/Euro	21	(27.6)	2	(3.5)			11	(17.7)	12	(16.9)	23	(17.3)
Maternal education					17.47	<.001						
Graduate	49	(64.5)	49	(86.0)			48	(77.4)	50	(70.4)	98	(73.7)
Non-graduate	24	(31.6)	1	(1.8)			12	(19.4)	13	(18.3)	25	(18.8)
Paternal education					11.58	.001						
Graduate	41	(53.9)	47	(82.5)			47	(75.8)	41	(57.7)	88	(66.2)
Non-graduate	17	(22.4)	2	(3.5)			7	(11.3)	12	(16.9)	19	(14.3)
Medical treatment					12.96	.000						
Inpatient	57	(75.0)	25	(43.9)			33	(53.2)	49	(69.0)	82	(61.7)
Outpatient	19	(25.0)	32	(56.1)			29	(46.8)	22	(31.0)	51	(38.3)
Days of hospital stay	3.46	(4.93)	6.16	(10.06)	-1.85	.068	4.10	(7.78)	5.14	(7.72)	4.66	(7.73)
Range		0 - 26		0 - 33				0 - 33		0 - 28		0 - 33
ISS	3.27	(3.48)	2.26	(2.09)	2.02	.046	2.59	(2.70)	3.01	(3.20)	2.82	(2.97)
Range		1 - 17		1 - 9				1 - 9		1 - 17		1 - 17
% TBSA burned	5.52	(4.98)	5.35	(5.59)	.14	.890	6.18	(6.21)	4.63	(4.22)	5.41	(5.35)
Range		0.5 – 17.0		1.0 – 30.0				0.5 – 30.0		0.5 – 21.0		0.5 – 30.0

Note. Euro = European, ISS = Injury Severity Score, TBSA = Total body surface area burned.

Characteristics of outcome variables including subscales at baseline, 3- and 6-months follow-up for intervention and control condition of the combined sample (N = 133) are depicted in **Table 14**. Significantly more children from the intervention group met full PTSD diagnostic criteria at baseline than control children (χ^2 = 5.13, p = .024). At 3-months, TAU children had significantly higher PTSS severity scores (t = 2.68, p = .009) and more functional impairment (χ^2 = 4.58, p = .032). Group differences regarding PTSD diagnosis at 6-months reached borderline significance (χ^2 = 4.77, p = .058), with the intervention group no longer having any PTSD diagnoses.

The effect of the CARE intervention on PTSS severity was evaluated using multilevel modelling. The null model included the intercept and a random effect for each child (random intercept). The following fixed effects were included stepwise in the model: (1) linear time, (2) group, (3) quadratic time, (4) interaction time x group, and (5) site (AUS or CH). Including the quadratic time improved the model significantly (χ^2 = 6.32, p = .012). In the last step, a random effect of time for each child (random slope) was included, significantly improving the model (χ^2 = 13.45, p = .001). Model estimates are presented in **Table 15**. The quadratic time x group interaction was significant (t = 3.08, p = .003), indicating a significant effect of the CARE intervention on PTSS severity over time. Further, the linear effect for time was significant (t = -5.77, p < .001), indicating that PTSS severity decreased in both groups over time. Site did not predict PTSS severity, but was retained in the model to account for any potential effect of site. Fixed effects explained 27.5% of the variance of the dependent variable PTSS severity. *Figure 8* shows that CARE children experienced a significantly quicker reduction in PTSS severity scores over the first 3-months compared to TAU children children (t = 2.64, p = .009), hence illustrating descriptively the curves following quadratic courses. However, at 6-months post-injury, the mean PTSS severity scores of both groups were not significantly different (t = 0.97, p = .335). Within-subject effect sizes for PTSS severity from baseline to 6-months were large for CARE (d = -1.17) and for TAU groups (d = - 0.89). A medium between-group effect size for PTSS severity was found at 3-months (d = 0.51) and small effect was found at 6-months (d = 0.19).

Table 14

Characteristics of outcome variables at baseline, 3 months- and 6 months follow-up for intervention and control condition of the combined sample ($N = 133$)

	Intervention group (n = 62)			Control group (n = 71)			Mean difference or odds ratio (95% CI)	*p* value
	n[a]	*M/n*	*SD/%*	*n*	*M/n*	*SD/%*		
Baseline PTSS								
Total severity score	59	24.90	15.23	67	23.94	15.09	0.96 (-4.40 to 6.32)	.724
Re-experiencing	61	8.70	6.54	68	7.88	6.19	0.82 (-1.40 to 3.04)	.466
Avoid. Neg. cog. mood	60	5.73	6.23	68	6.03	7.56	-0.30 (-2.74 to 2.14)	.808
Hyperarousal	60	10.17	6.30	69	10.00	5.45	0.17 (-1.88 to 2.22)	.870
Full diagnosis met	59	14	22.6	67	6	8.5	0.32 (0.11 to 0.89)	.024
Funct. impairment met	61	28	45.2	70	25	35.2	0.66 (0.33 to 1.32)	.236
Baseline behaviour diff.								
Total score	51	33.51	24.68	48	31.42	20.58	2.09 (-7.00 to 11.18)	.649
Internalizing score	51	9.22	10.07	48	8.08	7.21	1.14 (-2.37 to 4.65)	.521
Externalizing score	51	12.29	8.87	48	11.61	7.64	0.68 (-2.63 to 3.99)	.684
3-months PTSS								
Total severity score	52	11.02	10.42	57	17.30	13.94	-6.28 (-10.99 to -1.57)	.009
Re-experiencing	52	3.42	4.11	57	4.84	4.58	-1.42 (-3.08 to 0.24)	.093
Avoid. Neg. cog. mood	52	2.33	3.54	57	4.39	5.42	-2.06 (-3.82 to -0.30)	.022
Hyperarousal	52	5.23	6.32	57	8.07	6.95	-2.84 (-5.37 to -0.31)	.028
Full diagnosis met	47	2	3.2	54	6	8.5	2.94 (0.57 to 15.27)	.182
Funct. impairment met	47	7	11.3	54	18	25.4	2.86 (1.07 to 7.63)	.032
3-months behaviour diff.								
Total score	47	20.20	19.04	46	27.39	23.89	-7.19 (-16.08 to 1.70)	.112
Internalizing score	47	4.83	6.11	46	6.94	6.91	-2.11 (-4.80 to 0.58)	.122
Externalizing score	47	8.23	8.13	46	10.18	9.87	-1.95 (-5.67 to 1.77)	.301
6-months PTSS								
Total severity score	50	9.68	9.83	55	11.75	11.82	-2.07 (-6.30 to 2.16)	.335
Re-experiencing	50	3.10	3.48	55	3.31	4.31	-0.21 (-1.74 to 1.32)	.785
Avoid. Neg. cog. mood	50	2.24	4.11	55	2.11	3.88	0.13 (-1.42 to 1.68)	.868
Hyperarousal	50	4.34	5.22	55	6.33	5.85	-1.99 (-4.14 to 0.16)	.070
Full diagnosis met	45	0	0	48	5	7.0	*NA*	.058
Funct. impairment met	45	6	9.7	48	13	18.3	2.41 (0.83 to 7.04)	.100
6-months behaviour diff.								
Total score	46	17.93	21.54	49	16.12	15.79	1.81 (-5.85 to 9.47)	.640
Internalizing score	46	4.39	6.39	49	3.98	4.48	0.41 (-1.83 to 2.65)	.717
Externalizing score	46	7.04	8.62	49	6.00	6.39	1.04 (-2.04 to 4.12)	.504

Notes. Avoid. Neg. cog. mood = Avoidance and Negative alterations in cognitions and mood. Funct. = Functional. Diff. = Difficulties. NA = not applicable. PTSS = PTSD symptoms. [a]*n* is the number of children for whom means/SDs could be computed due to non-drop-out or non-missing data.

Table 15

Estimates of multilevel models for PTSS severity and total behaviour difficulties

	Estimate b	*Standard error*	*df*	*t*	*p*
PTSS severity					
(Intercept)	16.46	1.41	131.77	11.71	< .001
Time linear	- 104.28	18.07	127.78	- 5.77	< .001
Time quadratic	3.20	13.49	114.33	0.24	.813
Group (intervention)	-2.91	1.72	128.84	- 1.69	.093
Site (CH)	2.88	1.73	127.00	1.67	.098
Time linear x group	- 25.78	26.25	126.15	- 0.98	.328
Time quadratic x group	60.06	19.53	113.96	3.08	.003
Random Effects	*Variance*	*SD*	*Correlation*		
(Intercept)	*255.49*	*15.98*			
Time linear	*36.89*	*6.07*	*-.87*		
Residual variance	*76.88*	*8.77*			
Behaviour difficulties					
(Intercept)	26.56	3.12	108.47	8.50	<.001
Time linear	-128.30	22.91	93.97	-5.60	<.001
Time quadratic	-23.92	16.31	87.19	-1.47	.150
Group (intervention)	-0.76	3.64	106.93	-0.21	.835
Site (CH)	-2.29	3.61	106.01	-0.63	.528
Time linear x group	2.63	32.48	95.76	0.08	.936
Time quadratic x group	70.79	22.90	87.76	3.09	.003
Random Effects	*Variance*	*SD*	*Correlation*		
(Intercept)	639.25	25.28			
Time linear	50.07	7.08	-.72		
Residual variance	86.53	9.30			

Notes. PTSS severity: *N* = 133. Observations = 340. Deviance = 2660.2. BIC = 2724.3. Behaviour difficulties: *N* = 109. Observations = 287. Deviance = 2418.6. BIC = 2480.8.

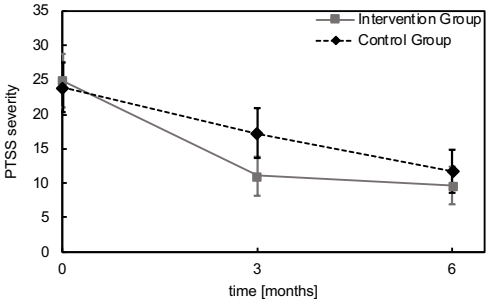

Figure 8. Trajectories of change across baseline, 3- and 6-months follow-ups, by treatment condition, for PTSS severity scores.

Table 16

Estimates of binary logistic multilevel regression models for PTSD diagnosis and functional impairment

	Estimate b	*Standard Error*	*z*	*p*
PTSD diagnosis				
(Intercept)	-9.59	1.93	-4.96	<.001
Time	0.12	0.52	0.24	.814
Group (intervention)	10.75	2.95	3.65	<.001
Site (CH)	0.45	1.37	0.33	.741
Time x group	-8.87	2.33	-3.80	<.001
Random Effects	*Variance*	*SD*		
(Intercept)	141.10	11.88		
Functional impairment				
(Intercept)	-0.31	0.48	-0.65	.516
Time	-0.20	0.22	-0.91	.363
Group (intervention)	1.29	0.71	1.82	.068
Site (CH)	-0.41	0.33	-1.26	.209
Time x group	-0.94	0.37	-2.50	.012
Random Effects	*Variance*	*SD*		
(Intercept)	0.94	0.97		

Notes. PTSD diagnosis: $N = 133$. Observations = 320. Deviance = 169.2. BIC = 203.8. Functional impairment: $N = 132$. Observations = 325. Deviance = 369.1. BIC = 403.8.

Binary logistic multilevel regression analyses to assess change in PTSD diagnosis and functional impairment included the fixed effects of time, group, time x group and site with a random intercept for patient **Table 16**. Both models revealed a significant time x group interaction, indicating a significant effect of the CARE intervention over time on both the number of PTSD diagnoses (z = -3.80, p < .001) and functional impairment (z = -2.50, p = .012). Descriptively, the numbers of PTSD diagnoses and functional impairment met deceased more in children in the intervention group than in control children, especially from baseline to 3-monts (**Table 14**).

The final model to analyse treatment group differences in behaviour difficulties over time (**Table 15**) included the same effects as for PTSS severity. The interaction quadratic time x group was significant (t = 3.09, p = .003), indicating a significant effect of the CARE intervention on behaviour difficulties over time. Independent of group allocation, behaviour difficulties significantly decreased in children from baseline to 6-months (t = -5.60, p < .001). Fixed effects explained 25.8% of the variance in behaviour difficulties. *Figure 9* shows the course of mean behaviour difficulties over time in both groups. Descriptivly, total behavioural difficulties did not reduce in control children during the first 3-months post-injury, whereas they reduced in children in the intervention group. While, no significant between-group differences were found for behaviour difficulties at 3- or 6-months (t = 1.61, p = .112; t = -0.47, p = .640), within-group pre-post effect sizes for behaviour difficulties were medium to large (CARE: d = -0.67, TAU: d = -0.84). The between-group effect sizes for 3- and 6-months were small (d = -0.33, d = -0.10). No adverse events were reported for either site.

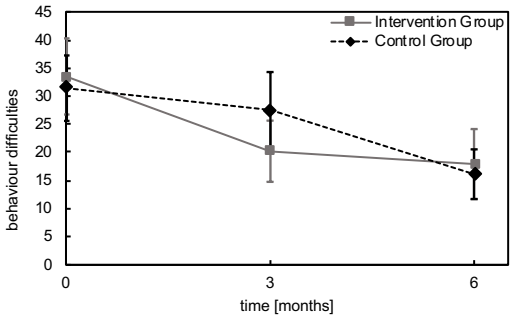

Figure 9. Trajectories of change across baseline, 3- and 6-months follow-ups, by treatment condition, for total behaviour difficulties.

Discussion

To date, there is limited and conflicting empirical evidence regarding the efficacy of providing early intervention for PTSD to children and adolescents, and no evidence currently exists for preventive interventions for trauma reactions in young children. This study aimed to address these gaps by developing and evaluating the efficacy of an early targeted intervention to reduce trauma reactions in young injured children (1–6 years). The combined results from a multi-site RCT conducted at major tertiary children's hospitals provide strong evidence that indicates the targeted preventive intervention was successful, facilitating faster recovery in young injured children. Specifically, in line with our primary hypothesis, the CARE-intervention revealed a significant effect on PTSS severity in young children over time. Intervention children experienced a significantly lower PTSS severity at 3-months compared to TAU children. However, this was not the case for the 6-months assessment. These results indicate that children receiving the CARE-intervention recovered more quickly. The secondary hypotheses were mostly supported as there was a significant effect of the CARE-intervention on rates of PTSD diagnosis rates over time. This is especially remarkable given there were significantly more PTSD diagnoses in the intervention (22.6%) vs control group (8.5%) at baseline but no (0%) diagnoses in the intervention group vs 7% in the control group by 6-months. CARE children also experienced less functional impairment in comparison to the TAU group from baseline (45.2% vs 35.2%) to 6-months (9.7% vs 18.3%). Again, the CARE-intervention was most helpful from baseline to 3-months. The CARE-intervention also lead to faster recovery from behavioural difficulties over 3-months post-injury.

This makes CARE the first known preventive psychological intervention to demonstrate efficacy in reducing and preventing persistent PTSS, PTSD, functional impairment, and behavioural difficulties in very young children up to 3-months following trauma. Only one RCT to date has found that an early intervention for older children (7–16 years) and parents was efficacious in reducing PTSD diagnoses and PTSS (Berkowitz et al., 2011). The only other study that has evaluated an early intervention for young injured children did not find the intervention to be effective (Kramer & Landolt, 2014).

Important key elements of CARE that might explain the success of this intervention include (1) timing and intensity of intervention, (2) delivery of intervention by psychologists (3) focus on supporting parents, (4) addressing symptoms specific to young children, e.g. tantrums, separation anxiety, and (5) using developmentally appropriate therapeutic resources for very young children. As current literature has shown that parents play an important role in children's posttraumatic adjustment (De Young et al., 2014; Haag & Landolt, 2017), CARE focused on providing parents with knowledge and tools to support their child as well as manage their own distress. Finally, anecdotal evidence from parents indicated the owl toy and the storybook were seen as very helpful resources. The rationale for the owl toy was to provide a possible transitional object to promote feelings of safety and comfort (Ybarra, Passman, & Eisenberg, 2000). The storybook was included to help children and parents to understand and process the accident and medical treatment in a safe way.

There are more noteworthy clinical implications from this current study. First, even though significant group differences for PTSS severity at 6-months were not found, it is clinically meaningful that children who received the CARE-intervention showed a significantly quicker recovery over the first 3-months. Trauma symptoms (e.g. sleep disturbance, intrusive memories) are very distressing for both the child and family and can cause significant impairment in daily functioning. Further, initial traumatic stress reactions are highly comorbid with and predictive of other types of disorders in young children (De Young et al., 2012). Therefore, the quicker these symptoms resolve the better for everyone. Reducing acute child PTSS may also help reduce pain, lead to better treatment adherence and physical outcomes during this key recovery period post-injury (Brown, Kenardy, & Dow, 2014; Gouin & Kiecolt-Glaser, 2011). The findings are also important given the rapid rate of development that can occur over relatively short periods during early childhood and that trauma exposure at a key stage can significantly derail a child's developmental trajectory. Additionally, including functional impairment as a secondary outcome measure is important as symptoms from PTSD diagnostic criteria in young children are still subject to debate and due to the fact that young children might react to trauma with a broad range of symptoms (De Young & Landolt, 2018).

Overall, the present study makes a significant contribution to the clinical and research evidence base and has many strengths. The results were found across two international sites where the intervention was conducted in different languages, an adequate sample size was obtained across a variety of injury types and advanced statistical analyses were adopted. However, some limitations must be considered. Due to slightly different inclusion criteria and recruitment procedures, the Australian and Swiss samples differed in age, type of injury and inpatient/outpatient treatment. However, the analyses considered these differences and did not find any site effects. Other potential limitations are that the majority of parents in this sample were Anglo/European and well-educated, which may reduce the generalisability of treatment findings to families with lower educational backgrounds and ethnic minorities. The intervention and control groups differed significantly for PTSD diagnoses at baseline. However, given that those in the intervention group had more PTSD diagnoses at baseline but none at 6-months follow-up, this difference is not considered to have a detrimental impact on the interpretation of our findings. Further, our comparison group was TAU rather than an attention placebo or active alternate intervention. However, both groups participated in screening and baseline assessments and it is possible that this alone can provide a helpful form of intervention (e.g. become aware of PTSS, reassurance, normalisation). Finally, outcomes were assessed via parent-reports only, thus leading to a possible source of bias. However, there are currently no other valid assessment options for this young age group.

Future research is needed to provide further evidence to support the CARE-intervention. As our predictor variables (time, group, site) only explained 27.5% and 25.8% of the respective outcome variable variances, this leaves room to explore potential mediators and moderators of treatment outcome. Further examination of this data is needed to determine if the intervention was also beneficial for reducing parental PTSS, guilt, and unhelpful trauma-related parenting behaviours. Future research could also look at cultural adaptations and evaluating efficacy for different single-event traumas (e.g. intensive care admission, violence, natural disasters).

In summary, trauma during early childhood has largely been neglected in research and clinical practice. This research is of considerable clinical significance and innovation as it is the first targeted preventive intervention to find effects of a faster recovery from trauma reactions in young children after exposure to an accidental trauma. Intervening during early childhood and immediately after a traumatic event, before problems become entrenched, has the potential to diminish the burden of disease and dysfunction across the lifespan. The successful dissemination and implementation of a preventive intervention for this at-risk

population is likely to have significant positive implications for reducing the social and economic costs associated with single-event trauma.

Declaration of interest

We declare no competing interests.

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